

posure; others remain asymptomatic, and later the condition begins to progress again. In many persons, the condition progresses gradually with formation of massive, upper lobe, bilateral lung opacities.

There is high incidence of lung cancer in vineyard workers using Bordeaux mixture. Vineyard sprayers' lung is best diagnosed by open or trephine lung biopsy; mediastinoscopy may prove to be helpful.

Preliminary inquiry showed that at least 340,000 pounds of copper compounds are used as agricultural pesticides in California each year. These consist of inorganic and organic copper compounds and mixtures.

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Evaluation and Treatment of a Solitary Lung Nodule

CONTROVERSY CONTINUES in the therapeutic management of noncalcified solitary lung nodules (6 cm or less). Diagnostic attempts are directed toward differentiating benign from malignant lesions, although malignancy is often suspected in 5 to 6 cm nodules. Definite diagnosis, short of operation, can not always be made; therefore, some authors studying this problem recommend the removal of all noncalcified coin lesions. Newer diagnostic techniques have aided evaluation before or instead of surgical procedures (small but definite rates of mortality and morbidity are associated with thoracotomy). With peripheral nodules, the incidence of carcinoma has been reported as being less than 20 percent when detection is the result of a routine x-ray film of the chest. A previous x-ray film of the chest for comparison is by far the most important diagnostic aid.

It is unusual for bronchogenic carcinoma to present as a solitary nodule in a patient under 35 years old. This fact may be in part attributable to

the biological growth patterns of various carcinomas. It has been proposed that the doubling time—that is, the amount of time it takes the tumor to double its volume—is relatively constant and specific for certain lung neoplasms. Thus, the tumor which shows a twofold enlargement on x-ray studies has in fact increased in volume eightfold. The doubling time has been estimated as being between 30 and 300 days and when one sees a coin lesion that is 1 cm in diameter, it is proposed that 30 doublings have occurred. Squamous cell carcinoma has a much more rapid doubling time than an adenocarcinoma. Therefore, these neoplasms have probably been present from 8 to 16 years before their presence is shown on a chest x-ray film. This is not to minimize the importance of a work-up of a noncalcified solitary nodule in a patient under 35 years old, but merely to point out the slim chance that such a lesion will be malignant in nature.

Whereas evaluation of the solitary nodule in all age groups is similar, the major concern is directed toward those patients over 35 years old. Diagnostic procedures, in addition to following the plain chest x-ray studies and tomography (which serves to rule out the presence of calcium and to disclose any extension of tendrils into the lung substance), include a sputum examination for cytology and bronchial brush and bronchoscopic biopsies using a fiberoptic bronchoscope. These latter two are done under direct fluoroscopic vision preferably using biplane fluoroscopy so that one can get peripherally into the solitary nodule. These techniques are being improved continually by radiologists and respiratory disease physicians and such biopsy information will be highly important to a thoracic surgeon before an open-lung excisional biopsy.

Finally, the needle aspiration technique, again under fluoroscopic control, is useful in skilled hands. There is a low rate of morbidity associated with this technique, and better than 80 percent positive results have been recorded. It has been suggested that the risk of tumor implant along the needle tract is rare and therefore that this technique is less likely to spread malignant cells than with the potential for spillage of tumor cells during an open incisional biopsy. Again, if the surgeon knows beforehand that the lesion is malignant, he can carry out a closed procedure without doing a biopsy at the time of operation.

When there are negative findings from a needle biopsy or brush and bronchoscopic biopsies which

produce no material of diagnostic quality, a solitary lung nodule still must be considered potentially malignant. The patient's age and clinical situation will dictate if an open biopsy or interval x-ray studies of the chest alone will be necessary.

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The Importance of 2,3-Diphosphoglycerate in Regulation of Tissue Oxygenation

THAT TISSUE OXYGENATION is dependent on more than just the arterial oxygen tension (PaO_2) and oxygen saturation is abundantly clear. The patient may have an excellent PaO_2 and oxygen (O_2) saturation, and yet have inadequate oxygenation at the tissue level due to a reduced hemoglobin (for example, reduced oxygen carrying capacity or O_2 content secondary to anemia). Oxygen delivery is as dependent on cardiac output as on O_2 content. The patient in shock may suffer from a tissue oxygen deficit due to inadequate tissue perfusion.

Another factor recognized many years ago is that the O_2 dissociation curve (relationship of O_2 saturation to PaO_2) may be shifted to the right or to the left. A shift of the curve to the right results in improved oxygen delivery by decreasing hemoglobin's affinity for O_2 . A shift of the curve to the left increases hemoglobin's affinity for O_2 resulting in impaired O_2 release to the tissue. Those factors which shift the curve to the left include hypothermia, hypocapnia and alkalosis, while fever, hypercapnia and acidosis result in a rightward shift of the curve. Certain congenital hemoglobins may present with either increased or decreased affinity for oxygen.

A red cell phosphate enzyme, 2,3-diphosphoglycerate (2,3-DPG), has recently been shown to be an important factor regulating tissue O_2 delivery.

An increased 2,3-DPG level decreases hemoglobin's affinity for O_2 , resulting in improved release of O_2 at the tissue level. A reduction in 2,3-DPG has the opposite effect. Factors resulting in an increased 2,3-DPG include hypoxia, anemia and thyrotoxicosis. Blood preserved with acid citrate dextrose (ACD) preservative loses up to 50 percent of its 2,3-DPG within 72 hours. If this blood is transfused, the hemoglobin will not release O_2 to the tissue properly because the O_2 dissociation curve is shifted to the left, an effect lasting up to 24 hours. Citrate phosphate dextrose (CPD) preserved blood, however, maintains 2,3-DPG levels much more effectively for two to three weeks.

P_{50} is a term now being used to indicate if the O_2 dissociation curve is shifted. Normal P_{50} (the PaO_2 when the O_2 saturation is 50 percent) is approximately 26.5 mm of mercury. An increased P_{50} would indicate a shift of the curve to the right.

The patient-care team should take all of these factors into consideration when evaluating the adequacy of tissue oxygenation. For instance, correction of alkalosis in itself will improve O_2 delivery to the tissues.

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Rifampin in the Treatment of Tuberculosis

RIFAMPIN (United States Adopted Name) or rifampicin (World Health Organization nonproprietary name) has proven to be a very effective addition to the list of antituberculosis agents. A semisynthetic derivative of an antibiotic recovered in 1957 by Italian researchers from a strain of *Streptomyces mediterranei*, rifampin has been shown to have a wide range of biologic activities in such diverse life forms as viruses, bacteria and mammals. When combined, isoniazid and rifampin have a remarkable ability to kill *Mycobacterium tuberculosis*, and to sterilize infected tissues in animal models. Trials in man have shown that the combination of isoniazid and rifampin is at least as effective as any previous combination of agents used, and has the added advantage of excellent patient tolerance. Rifampin in combination with other antituberculosis agents has proven highly effective in both short-course treatment